We Claim:

1. A solid pharmaceutical dosage form for oral administration, the dosage form comprising:
an extended release layer comprising a biguanide; and
an immediate release layer comprising a glitazone.

2. The dosage form of claim 1, wherein the biguanide comprises one or more of metformin, phenformin, and buformin.

3. The dosage form of claim 1, wherein the biguanide is metformin.

4. The dosage form of claim 1, wherein the glitazone comprises one or more of pioglitazone, rosiglitazone, troglitazone, ciglitazone and englitazone.

5. The dosage form of clam 4, wherein the glitazone is pioglitazone.

6. The dosage form of claim 1, wherein after oral administration the biguanide is released over a period of about 4 to about 36 hours.

7. The dosage form of claim 6, wherein the biguanide is released over a period of about 8 to about 24 hours.

8. The dosage form of claim 1, wherein the dosage form comprises tablets or capsules.

9. The dosage form of claim 8, wherein the tablet includes a coating.

10. The dosage form of claim 8, wherein the capsules include one or more of pellets, beads, granules, multiparticulates, tablets and powder.

11. The dosage form of claim 1, wherein the extended release layer comprises a matrix.

12. The dosage form of claim 11, wherein the matrix comprises a uniform mixture of the biguanide and one or more rate controlling polymers.

13. The dosage form of claim 12, wherein the one or more rate-controlling polymers comprises hydrophilic polymers, hydrophobic polymers, or a combination thereof.

14. The dosage form of claim 11, wherein the matrix further comprises one or more pharmaceutically acceptable excipients.

15. The dosage form of claim 14, wherein the pharmaceutically acceptable excipients comprise one or more of diluents, lubricants, disintegrants, binders, glidants, coloring and flavoring agents.

16. The dosage form of claim 1, wherein the biguanide is layered onto a pharmaceutically inert core or seed.

17. The dosage form of claim 16, wherein the inert core or seed is hydrosoluble or hydroinsoluble.

18. The dosage form of claim 1, wherein the immediate release outer layer further comprises film-forming polymers and optionally other pharmaceutically acceptable excipients.

19. The dosage form of claim 18, wherein the film-forming polymers are water–soluble polymers.

20. The dosage form of claim 18, wherein the pharmaceutically acceptable excipients comprises one or more of plasticizers, opacifiers and colorants.

21. The dosage form of claim 1, further comprising one or more of sulfonylurea, insulin, alpha-glucosidase inhibitors, meglitinides, fibrates, statins, squalene synthesis inhibitors and angiotensin-converting enzyme inhibitors.

22. The dosage form of claim 1, further comprising a wetting agent in the immediate release layer, wherein the immediate release layer comprises the glitazone and the wetting agent in a weight ratio ranging from about 10:1 to about 1:25.

23. The dosage form of claim 22, wherein the wetting agent is selected from amongst hydrophilic and hydrophobic surfactants.

24. The dosage form of claim 23, wherein the hydrophilic surfactants are selected from one or more of non-ionic surfactants, ionic surfactants or mixtures thereof.

25. The dosage form of claim 23, wherein the hydrophobic surfactants are selected from one or more of alcohols; polyoxyethylene alkylethers; fatty acids; glycerol fatty acid monoesters; glycerol fatty acid diesters; acetylated glycerol fatty acid monoesters; acetylated glycerol fatty acid diesters, lower alcohol fatty acid esters; polyethylene glycol fatty acid esters; polyethylene glycol glycerol fatty acid esters; polypropylene glycol fatty acid esters; polyoxyethylene glycerides; lactic acid derivatives of monoglycerides; lactic acid derivatives of diglycerides; propylene glycol diglycerides; sorbitan fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers, polyethyleneglycols as esters or ethers, polyethoxylated castor oil; polyethoxylated hydrogenated castor oil, polyethoxylated fatty acid from castor oil or polyethoxylated fatty acid from castor oil or polyethoxylated fatty acid from hydrogenated castor oil.

26. The dosage form of claim 24, wherein the non-ionic surfactants are selected from one or more of alkylglucosides; alkylmaltosides; alkylthioglucosides; lauryl macrogolglycerides; caprylocaproyl macrogolglycerides, polyoxyethylene alkyl ethers; polyoxyethylene alkylphenols; polyethylene glycol fatty acid esters; polyethylene glycol glycerol fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers; polyglycerol fatty acid esters; polyoxyethylene glycerides; polyoxyethylene sterols, derivatives, and analogues thereof; polyoxyethylene vegetable oils; polyoxyethylene hydrogenated vegetable oils; reaction products of polyols and at least one member of the group consisting of fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols; sugar esters, sugar ethers; sucroglycerides; and mixtures thereof.

27. The dosage form of claim 24, wherein the ionic surfactants are selected from one or more of alkyl ammonium salts; bile acids and salts, analogues, and derivatives thereof; fatty acid derivatives of amino acids, oligopeptides, and polypeptides; glyceride derivatives of amino acids, oligopeptides, and polypeptides; acyl lactylates; monoacetylated tartaric acid esters of monoglycerides, monoacetylated tartaric acid esters of diglycerides, diacetylated tartaric acid esters of monoglycerides, diacetylated tartaric acid esters of diglycerides; succinylated monoglycerides; citric acid esters of monoglycerides; citric acid esters of diglycerides; alginate salts; propylene glycol alginate; lecithins and hydrogenated lecithins; lysolecithin and hydrogenated lysolecithins; lysophospholipids and derivatives thereof; phospholipids and derivatives thereof; salts of alkylsulfates; salts of fatty acids; sodium docusate; and mixtures thereof.

28. The dosage form of claim 1, wherein the extended release layer comprises a core and the immediate release layer covers at least a portion of the core.

29. The dosage form of claim 1, wherein the dosage form comprises a bilayered dosage form.

30. A process for preparing a solid, orally administered pharmaceutical dosage form of an extended release core of a biguanide and an immediate release layer of a glitazone, the process comprising:

a. dispersing the biguanide in a solid matrix to form a core having a surface; and
b. layering the immediate release layer of the glitazone on the surface of the core.

31. The process of claim 30, wherein layering the immediate release layer further comprises layering one or more wetting agents.

32. The process of claim 31, wherein the glitazone and the one or more wetting agents are present in the immediate release layer in a weight ratio ranging from about 10:1 to about 1:25.

33. The process of claim 31, wherein the one or more wetting agents are selected from amongst hydrophilic or hydrophobic surfactants.

34. The process of claim 33, wherein the hydrophilic surfactants are selected from one or more of non-ionic surfactants, ionic surfactants or mixtures thereof.

35. The process of claim 33, wherein the hydrophobic surfactants are selected from one or more of alcohols; polyoxyethylene alkylethers; fatty acids; glycerol fatty acid monoesters; glycerol fatty acid diesters; acetylated glycerol fatty acid monoesters; acetylated glycerol fatty acid diesters, lower alcohol fatty acid esters; polyethylene glycol fatty acid esters; polyethylene glycol glycerol fatty acid esters; polypropylene glycol fatty acid esters; polyoxyethylene glycerides; lactic acid derivatives of monoglycerides; lactic acid derivatives of diglycerides; propylene glycol diglycerides; sorbitan fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers, polyethyleneglycols as esters or ethers, polyethoxylated castor oil; polyethoxylated hydrogenated castor oil, polyethoxylated fatty acid from castor oil or polyethoxylated fatty acid from castor oil or polyethoxylated fatty acid from hydrogenated castor oil.

36. The process of claim 34, wherein the non-ionic surfactants are selected from one or more of alkylglucosides; alkylmaltosides; alkylthioglucosides; lauryl macrogolglycerides; caprylocaproyl macrogolglycerides, polyoxyethylene alkyl ethers; polyoxyethylene alkylphenols; polyethylene glycol fatty acid esters; polyethylene glycol glycerol fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers; polyglycerol fatty acid esters; polyoxyethylene glycerides; polyoxyethylene sterols, derivatives, and analogues thereof; polyoxyethylene vegetable oils; polyoxyethylene hydrogenated vegetable oils; reaction products of polyols and at least one member of the group consisting of fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols; sugar esters, sugar ethers; sucroglycerides; and mixtures thereof.

37. The process of claim 34, wherein the ionic surfactants are selected from one or more of alkyl ammonium salts; bile acids and salts, analogues, and derivatives thereof; fatty acid derivatives of amino acids, oligopeptides, and polypeptides; glyceride derivatives of amino acids, oligopeptides, and polypeptides; acyl lactylates; monoacetylated tartaric acid esters of monoglycerides, monoacetylated tartaric acid esters of diglycerides, diacetylated tartaric acid esters of monoglycerides, diacetylated tartaric acid esters of diglycerides; succinylated monoglycerides; citric acid esters of monoglycerides; citric acid esters of diglycerides; alginate salts; propylene glycol alginate; lecithins and hydrogenated lecithins; lysolecithin and hydrogenated lysolecithins; lysophospholipids and derivatives thereof; phospholipids and derivatives thereof; salts of alkylsulfates; salts of fatty acids; sodium docusate; and mixtures thereof.

38. The process of claim 30, wherein the biguanide is selected from one or more of metformin, phenformin and buformin.

39. The process of claim 30, wherein the biguanide comprises metformin.

40. The process of claim 30, wherein the glitazone is selected from one or more of pioglitazone, rosiglitazone, troglitazone, ciglitazone and englitazone.

41. The process of clam 30, wherein the glitazone comprises pioglitazone.

42. The process of claim 30, wherein after oral administration the biguanide is released over a period of about 4 to about 36 hours.

43. The process of claim 42, wherein the biguanide is released over a period of about 8 to about 24 hours.

44. The process of claim 30, further comprising forming a tablet or a capsule.

45. The process of claim 44, further comprising coating the tablet.

46. The process of claim 44, wherein the capsule contains one or more of pellets, beads, granules, multiparticulates, tablets and powder.

47. The process of claim 48 wherein the core comprises a matrix.

48. The process of claim 30, wherein the matrix comprises a uniform mixture of the biguanide and one or more rate controlling polymers.

49. The process of claim 48, wherein the one or more rate-controlling polymers may be either or both of hydrophilic and hydrophobic.

50. The process of claim 30, wherein the matrix further comprises one or more pharmaceutically acceptable excipients.

51. The process of claim 50, wherein the pharmaceutically acceptable excipients comprise one or more of diluents, lubricants, disintegrants, binders, glidants, colorants, and flavorants.

52. The process of claim 30, wherein the biguanide is layered onto pharmaceutically inert core or seeds.

53. The process of claim 52, wherein the inert core or seeds are hydrosoluble or hydroinsoluble.

54. The process of claim 30, wherein the immediate release outer layer further comprises film-forming polymers and optionally other pharmaceutically acceptable excipients.

55. The process of claim 54, wherein the film-forming polymers comprise water–soluble polymers.

56. The process of claim 54, wherein the pharmaceutically acceptable excipients comprise one or more of plasticizers, opacifiers and colorants.

57. The process of claim 30, further comprising placing a seal-coat over the core, wherein the seal-coat comprises hydrophilic polymers.

58. A process for preparing a bilayered, solid, orally administered pharmaceutical dosage form of a biguanide and a glitazone, the process comprising:

a. dispersing the biguanide in an extended release carrier base material;
b. separately dispersing the glitazone in an immediate release carrier base material; and
c. compressing the material of step a and step b to form bilayered tablet.

59. The process of claim 58, wherein the immediate release carrier base material further comprises one or more wetting agents before or after dispersing the glitazone.

60. The process of claim 59, wherein the glitazone and the one or more wetting agents are present in a weight ratio ranging from about 10:1 to about 1:25.

61. The process of claim 59, wherein the one or more wetting agents are selected from amongst hydrophilic or hydrophobic surfactants.

62. The process of claim 61, wherein the hydrophilic surfactants are selected from one or more of non-ionic surfactants, ionic surfactants or mixtures thereof.

63. The process of claim 61, wherein the hydrophobic surfactants are selected from one or more of alcohols; polyoxyethylene alkylethers; fatty acids; glycerol fatty acid monoesters; glycerol fatty acid diesters; acetylated glycerol fatty acid monoesters; acetylated glycerol fatty acid diesters, lower alcohol fatty acid esters; polyethylene glycol fatty acid esters; polyethylene glycol glycerol fatty acid esters; polypropylene glycol fatty acid esters; polyoxyethylene glycerides; lactic acid derivatives of monoglycerides; lactic acid derivatives of diglycerides; propylene glycol diglycerides; sorbitan fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers, polyethyleneglycols as esters or ethers, polyethoxylated castor oil; polyethoxylated hydrogenated castor oil, polyethoxylated fatty acid from castor oil or polyethoxylated fatty acid from castor oil or polyethoxylated fatty acid from hydrogenated castor oil.

64. The process of claim 62, wherein the non-ionic surfactants are selected from the one or more of alkylglucosides; alkylmaltosides; alkylthioglucosides; lauryl

macrogolglycerides; caprylocaproyl macrogolglycerides, polyoxyethylene alkyl ethers; polyoxyethylene alkylphenols; polyethylene glycol fatty acid esters; polyethylene glycol glycerol fatty acid esters; polyoxyethylene sorbitan fatty acid esters; polyoxyethylene-polyoxypropylene block copolymers; polyglycerol fatty acid esters; polyoxyethylene glycerides; polyoxyethylene sterols, derivatives, and analogues thereof; polyoxyethylene vegetable oils; polyoxyethylene hydrogenated vegetable oils; reaction products of polyols and at least one member of the group consisting of fatty acids, glycerides, vegetable oils, hydrogenated vegetable oils, and sterols; sugar esters, sugar ethers; sucroglycerides; and mixtures thereof.

65. The process of claim 62, wherein the ionic surfactants are selected from one or more of alkyl ammonium salts; bile acids and salts, analogues, and derivatives thereof; fatty acid derivatives of amino acids, oligopeptides, and polypeptides; glyceride derivatives of amino acids, oligopeptides, and polypeptides; acyl lactylates; monoacetylated tartaric acid esters of monoglycerides, monoacetylated tartaric acid esters of diglycerides, diacetylated tartaric acid esters of monoglycerides, diacetylated tartaric acid esters of diglycerides; succinylated monoglycerides; citric acid esters of monoglycerides; citric acid esters of diglycerides; alginate salts; propylene glycol alginate; lecithins and hydrogenated lecithins; lysolecithin and hydrogenated lysolecithins; lysophospholipids and derivatives thereof; phospholipids and derivatives thereof; salts of alkylsulfates; salts of fatty acids; sodium docusate; and mixtures thereof.

66. The process of claim 58, wherein the biguanide is selected from one or more of metformin, phenformin and buformin.

67. The process of claim 58, wherein the biguanide comprises metformin.

68. The process of claim 58, wherein the glitazone is selected from one or more of pioglitazone, rosiglitazone, troglitazone, ciglitazone and englitazone.

69. The process of clam 58, wherein the glitazone comprises pioglitazone.

70. The process of claim 58, wherein after oral administration the biguanide is released over a period of about 4 to about 36 hours.

71. The process of claim 70, wherein the biguanide is released over a period of about 8 to about 24 hours.

72. The process of claim 58, further comprising forming a tablet or a capsule.

73. The process of claim 72, further comprising coating the tablet.

74. The process of claim 72, wherein the capsule contains one or more of pellets, beads, granules, multiparticulates, tablets and powder.

75. The process of claim 58, wherein the biguanide layer comprises a matrix.

76. The process of claim 75, wherein the matrix comprises a uniform mixture of the biguanide and one or more rate controlling polymers.

77. The process of claim 76, wherein the one or more rate-controlling polymers may be either or both of hydrophilic and hydrophobic.

78. The process of claim 75, wherein the matrix further comprises one or more pharmaceutically acceptable excipients.

79. The process of claim 78, wherein the pharmaceutically acceptable excipients comprise one or more of diluents, lubricants, disintegrants, binders, glidants, colorants, and flavorants.

80. The process of claim 58, wherein the biguanide is layered onto pharmaceutically inert core or seeds.

81. The process of claim 80, wherein the inert core or seeds are hydrosoluble or hydroinsoluble.

82. The process of claim 58, wherein the immediate release carrier base material further comprises film-forming polymers and optionally other pharmaceutically acceptable excipients.

83. The process of claim 82, wherein the film-forming polymers comprise water-soluble polymers.

84. The process of claim 82, wherein the pharmaceutically acceptable excipients comprise one or more of plasticizers, opacifiers and colorants.

85. The process of claim 58, further comprising providing a seal-coat of one or more hydrophilic polymers between the two layers.

86. A method of treating non-insulin dependent diabetes mellitus in a patient in need thereof, the method comprising administering a solid, pharmaceutical dosage form of the combination of a biguanide and a glitazone, wherein the dosage form provides an extended-release of the biguanide and an immediate release of the glitazone.

87. The method of claim 86, wherein the biguanide comprises one or more of metformin, phenformin, and buformin.

88. The method of claim 86, wherein the biguanide is metformin.

89. The method of claim 86, wherein the glitazone comprises one or more of pioglitazone, rosiglitazone, troglitazone, ciglitazone and englitazone.

90. The method of clam 86 wherein the glitazone is pioglitazone.

91. The method of claim 86, wherein after oral administration the biguanide is released over a period of about 4 to about 36 hours.

92. The method of claim 86, wherein the biguanide is released over a period of about 8 to about 24 hours.

93. The method of claim 86, wherein the dosage form comprises tablets or capsules.

94. The method of claim 86, wherein the dosage form further comprises one or more of sulfonylurea, insulin, alpha-glucosidase inhibitors, meglitinides, fibrates, statins, squalene synthesis inhibitors and angiotensin-converting enzyme inhibitors.